

Patent claims

1. Sequence of the human beta2-adrenergic receptor gene wherein the bases have been substituted completely or partly in the positions 159, 245, 565, 934, 1120, 1221, 1541, 1568, ~~1633, 1666, 1839, 2078, 2110, 2640 and 2826.~~
2. Sequence according to claim 1 wherein it involves completely or partly the substitution of bases T -> A (position 159), A -> G (position 245), G -> A (position 565), G -> A (position 934), G -> C (position 1120), C -T (position 1221), C -> T (position 1541), T -> C (position 1568), A -> G (position 1633), C -> G (position 1666), G -> A, (position 1839), C -> T (position 2078), C -> A (position 2110), G -> C (position 2640) and G -> A (position 2826).
3. Sequence according to claims 1 and 2 characterized by the mutations 1541 T, 1633 A and 1666 C.
4. Sequence according to claims 1 and 2 characterized by the mutations 1541 C, 1633 G and 1666 G.
5. Sequence according to claims 1 and 2 characterized by the mutations 1541 T, 1633 G and 1666 C.
6. Sequence according to claims 1 and 2 characterized by the mutations 1541 T, 1568 T, 1633 A and 1666 C.
7. Sequence according to claims 1 and 2 characterized by the mutations 1541 C, 1568 C, 1633 G and 1666 G.
8. Sequence according to claims 1 and 2 characterized by the mutations 1541 T, 1568 T, 1633 G and 1666 C.

Method for determining dispositions to diseases wherein the DNA of a proband is extracted and genotyped at least in one of the substituted positions and subsequently compared with the reference DNA sequence, if necessary, with all potential

Art D2 combinations of variants from the individual mutation to all potential combinations of all variants being included, including any absolute number of variants.

10. Method according to claim 9 wherein the DNA of a proband is extracted and genotypified at least in position 1633.
11. Method according to claim 9 wherein the DNA of a proband is extracted and genotypified at least in the three positions 1541, 1633 and 1666.
12. Method according to claim 9 wherein the DNA of a proband is extracted and genotypified at least in the four positions 1541, 1568, 1633 and 1666.
13. Method according to claim 9 wherein the DNA of a proband is extracted and genotypified at least in the seven positions 245, 565, 934, 1541, 1568, 1633 and 1666.
- A 14. Method according to claims 9 or 12 wherein the positions 1541, 1568, 1633 and 1666 are genotypified.
15. Method according to claim 14 wherein at least 3 of the 4 positions 1541, 1568, 1633 and 1666 are genotypified.
- A 16. Method for determining the dispositions to diseases according to the claims 9, 14 or 15 wherein the positions 1541, 1633 and 1666 are genotypified.
- A 17. Method according to one of the claims 9 to 16 wherein genotypifying is brought about by sequencing or other methods suited for detecting variants.
- A 18. Methods according to one of the claims 9 to 17 for determining a disposition to high blood pressure and deviations of the blood pressure from the standard and other cardiovascular diseases including myocardial infarct and apoplexy; for determining a disposition to neuropsychiatric diseases such as depression, anxiety syndromes, attention deficit disorder with hyperactivity, eating disorder, e.g. anorexia nervosa and bulimia or disorders caused by post-traumatic stress; for determining a disposition to

diseases of the autonomic nervous system such as e.g. Bradbury-Eggleson, Sky-Drager and Riley-Day syndromes and dispositions to selective noradrenergic and baroreceptors or migraine; for determining a disposition to allergic diseases, in particular asthma and atopic disorder; for determining a disposition to metabolic diseases such as obesity and family "morbid obesity", including a prediction of the weight area as such or a disposition to a change of weight, including a prediction of the proportion of the measurements of the body as such as expressed e.g. in the "body mass index" (BMI).

A 19. Method according to one of the claims ~~9 to 17~~ for determining an individually different reactivity of the autonomic nervous system, in particular to endogenous and exogenous stress.

A 20. Method according to claim 19 for determining an individually different disposition to modification/deflections of blood pressure and/or heart rate caused by endogenous and exogenous stress or an individually different sensitivity/resistance to salt.

A 21. Method according to one of the claims ~~9 to 17~~ for determining the course and the degree of severity of diseases such as e.g. mentioned in claim 18, e.g. of neuropsychiatric diseases such as depression and anxiety syndromes, of cardiovascular diseases including myocardial infarct and apoplexy, of diseases of the autonomic nervous system and allergic diseases such as e. g. asthma.

A 22. Method according to one of the claims ~~9 to 17~~ for determining a disposition to metabolic diseases such as obesity.

A 23. Methods according to one of the claims ~~9 to 17~~ for predicting the survival time after severe diseases such as after a myocardial infarct, cardiac failure and/or apoplexy.

A 24. Use of sequence variants according to claims ~~1 to 8~~ for developing therapeutic agents and/or lifestyle drugs.

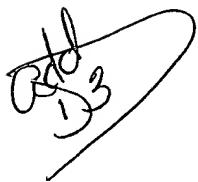
25. Use according to claim 24 for developing a new class of therapeutic agents directed to the beta2 receptor gene and attacking the 5' regulatory area, the promoter area and the

leader peptide, active via the regulation of transcription and translation, and by affecting their efficiency, notably by regulating the expression.

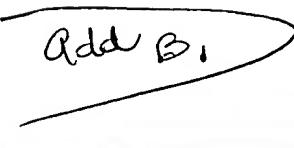
26. Use according to claim 24 for developing beta2 receptor agonists and antagonists, in particular individually specific beta2 receptor agonists and antagonists.
- A 27. Use according to one of the claims ~~9 to 17~~ for predicting the individually different responsiveness to so far known therapeutic agents such as beta2 receptor ligands and therapeutic agents developed in future also under claims 24 to 26 and the individually different responsiveness to the endogenous ligands adrenalin and noradrenalin.
- A 28. Use according to one of the claims ~~9 to 17~~ for predicting the individual habituation to the administration of pharmaceutical agents (tachyphylaxis) and a different disposition to side effects of pharmaceutical agents.
- A 29. Use according to one of the claims ~~9 to 17~~ to optimize the individual therapy or intervention directed to the beta2 receptor and its gene.
- A 30. Use of sequence variants according to claims ~~1 to 8 to~~ build up genes or vectors, in particular to develop pharmaceutically relevant substances.
- A 31. Use according to claims ~~24 to 30~~ for developing a diagnostic kit or an optional method for genotyping.
- A 32. Use according to claims ~~24 to 31~~ for developing a diagnostic kit for predicting the individual responsiveness to various beta2 receptor agonists and antagonists and to any newly developed beta2 active therapeutic agents, in particular also according to claim 25; for predicting the therapeutic efficiency of pharmaceutical agents the action mechanism of which involves modifications of the beta2 receptor structure, regulation or expression; for predicting the individually different responsiveness to the endogenous ligands adrenalin and noradrenalin; for predicting the individual habituation to pharmaceutical agents administered – tachyphylaxis – and a different disposition to side

effects of pharmaceutical agents; for optimizing the individual therapy or intervention to the beta2 receptor and its gene.

A 33. Use according to claims ~~1 to 8 and 9 to 32~~ for developing in vitro (e.g. cell cultures) and in vivo (e.g. transgenic animals) test systems expressing individual forms of the beta2 receptor gene, with the test systems serving to investigate the pathophysiology of diseases of in general medically important properties, with the beta2 receptor gene participating, and for developing and testing individually specific therapeutic agents agents and "lifestyle drugs" and substances directed to beta2 in general.



BS 153



Add B.